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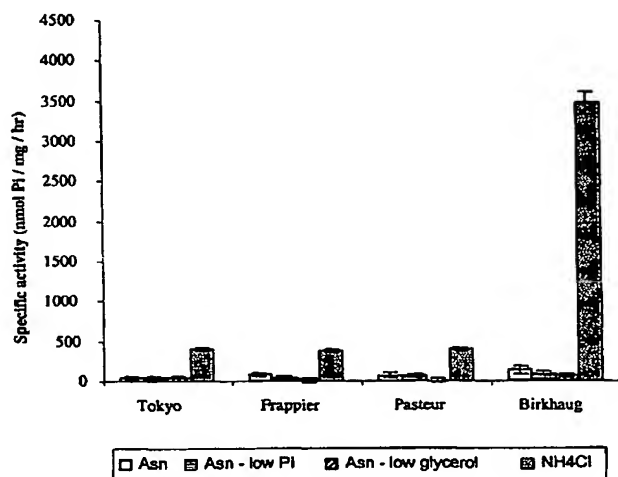
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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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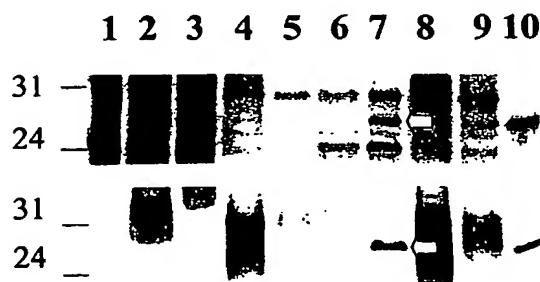
(54) Title: SECRETED ACID PHOSPHATASE (SAPM) IS PRESENT ONLY IN PATHOGENIC MYCOBACTERIA AND EXPRESSED SELECTIVELY AT ACIDIC PH

A



(57) Abstract: The invention relates to an isolated DNA construct, comprising a mycobacterium secreted acid phosphatase promoter or promoter fragment which is inducible by low pH. This invention further relates to diagnostic methods and vaccines for treatment or prophylaxis of pathogenic mycobacterial disease or infection. This invention also provides for methods of screening for compounds capable of modulating the activity, production or secretion of a mycobacterium secreted acid phosphatase.

B





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— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/01554

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N9/16 C12N15/55 C12N15/67 C12N5/10 C07K16/12
G01N33/50 A61K39/04 C12N15/52

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

BIOSIS, WPI Data, EPO-Internal, SEQUENCE SEARCH, EMBL, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SALEH MAZEN T ET AL: "Secretion of an acid phosphatase (SapM) by Mycobacterium tuberculosis that is similar to eukaryotic acid phosphatases" JOURNAL OF BACTERIOLOGY, vol. 182, no. 23, December 2000 (2000-12), pages 6850-6853, XP002275003 ISSN: 0021-9193 cited in the application the whole document --- -/--	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the International filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the International filing date but later than the priority date claimed

T later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the International search

25 March 2004

Date of mailing of the International search report

16/04/2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/01554

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! standard; genomic DNA; PRO; 16465 BP, 2 September 2002 (2002-09-02) FLEISCHMANN ET AL. : "Mycobacterium tuberculosis CDC1551, section 235 of 280 of the complete genome" Database accession no. AE007149 XP002275007 only the relevant sequence data is provided the whole document	1-30
X	COLE S T ET AL: "Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 393, 11 June 1998 (1998-06-11), pages 537-544, XP002087941 ISSN: 0028-0836 cited in the application the whole document	1-30
A	TRICCAS JAMES A ET AL: "Life on the inside: Probing Mycobacterium tuberculosis gene expression during infection" IMMUNOLOGY AND CELL BIOLOGY, vol. 78, no. 4, August 2000 (2000-08), pages 311-317, XP002275004 ISSN: 0818-9641 cited in the application the whole document	1-30
A	KUEHNEL M P ET AL: "Characterization of the intracellular survival of Mycobacterium avium ssp. paratuberculosis: phagosomal pH and fusogenicity in J774 macrophages compared with other mycobacteria." CELLULAR MICROBIOLOGY. ENGLAND AUG 2001, vol. 3, no. 8, August 2001 (2001-08), pages 551-566, XP002275005 ISSN: 1462-5814 cited in the application the whole document	1-30

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/01554

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>FISHER MARK A ET AL: "Microarray analysis of the Mycobacterium tuberculosis transcriptional response to the acidic conditions found in phagosomes" JOURNAL OF BACTERIOLOGY, vol. 184, no. 14, July 2002 (2002-07), pages 4025-4032, XP002275006 ISSN: 0021-9193 cited in the application the whole document</p>	1-30
A	<p>WO 01 81422 A (MAX PLANCK GESELLSCHAFT ;KOUL ANIL (DE); ULLRICH AXEL (DE)) 1 November 2001 (2001-11-01) claims 1-24</p>	10-30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/01554

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10-15 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-30 all partially

Isolated DNA sequence (Seq ID No 9) encoding the secreted protein with Seq ID No 10 and the promoter sequence with Seq ID No 1. Sequences hybridizing to said promoter sequence under high stringency hybridization conditions. Expression vector comprising said promoter sequences. Host cells transformed with said vector. Transcription cassettes comprising said promoter sequences. Methods of diagnosis by detecting the secreted acid phosphatase protein or encoding sequence. Method of screening for compounds modulating the production of the protein, or the activity of said protein, or the secretion of said protein. Kits for the detection of the protein or encoding sequence or promoter sequence. Antibodies specific for the encoded protein and vaccines comprising said antibody. Vaccines comprising the protein or fragments thereof, and vaccines comprising the promoter sequence. Antigenic composition comprising the polypeptide.

2. Claims: 1-30 all partially

As outlined for subject 1, but now for the polypeptide with Seq ID No 12, encoding polynucleotide with Seq ID No 11 and promotersequence with Seq ID No 2.

3. Claims: 1-30 all partially

As outlined for subject 1, but now for the polypeptide with Seq ID No 14, encoding polynucleotide with Seq ID No 13 and promotersequence with Seq ID No 3.

4. Claims: 1-30 all partially

As outlined for subject 1, but now for the polypeptide with Seq ID No 16, encoding polynucleotide with Seq ID No 15 and promotersequence with Seq ID No 4.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 03/01554

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0181422	A	01-11-2001	AU 6735801 A	07-11-2001
			WO 0181422 A1	01-11-2001
			EP 1274732 A1	15-01-2003
			US 2003180304 A1	25-09-2003